

§Appl. No. 09/856,044  
Amdt. dated August 11, 2004  
Reply to Office Action of, May 13, 2004

### **REMARKS**

Support for claims 12-13 can be found throughout the specification, e.g., on Page 7, lines 10-30.

#### **Rejection under §112, first paragraph**

Since the filing of the patent application, the claimed methods have been utilized successfully on nine different organisms. These include: *Helicobacter pylori* 26695 [P. Demirev, F. Pineda, J. Lin, C. Fenselau, Anal.Chem 73 (2001), 4566-4573, "Bioinformatics and mass spectrometry for microorganism identification: Proteome-wide post-translational modifications and database search algorithms for characterization of intact H. pylori"]; *Bacillus subtilis* B459; *Bacillus stearothermophilus* 467; *Acinetobacter calcoaceticus* ATCC 19606; *Haemophilus influenza* ATCC 9007; *Salmonella typhimurium* ATCC 14028; *Micrococcus luteus* ATCC 43981; *Pseudomonas aeruginosa* ATCC 27853; *Escherichia coli* ATCC 25922 [F. Pineda, M. Antoine, P. Demirev, A. Feldman, J. Jackman, M. Longenecker, J. Lin, Anal.Chem 75 (2003), 3817-3822 "Rapid Microorganism Identification by MALDI Mass Spectrometry and Model-derived Ribosomal Protein Biomarkers"]. See, attached publications. It is believed that these examples are more than adequate to establish that the claims are enabled for their complete scope.

The Pineda et al. (2003) publication identifies problems for prior art methods (e.g., Wang et al.) which are addressed by the claimed methods. See, e.g., Page 3817, first and second full paragraphs.

#### **Rejection under §103**

Applicants respectfully traverse the rejection of the claims as allegedly obvious over Wang et al. in view of Yates.

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Wang et al. do not disclose searching a sequence database for a plurality of intact, undigested proteins. Compare claims 1 and 13. The database described in Wang et al. is generated by mass spectrometry experiments and contains only mass spectral data. They specifically state: "With optimization of sample treatment/analysis methodologies is accomplished, it will become possible to begin to identify with confidence species-, genus- and strain-specific protein biomarkers through the development of sufficiently large libraries of bacterial protein mass spectra data." Page 463, Column 1. Thus, Wang et al. envision the construction of large libraries of information collected from mass spectroscopy studies to use as a tool in bacterial identification.

There is no disclosure in either Wang et al. or Yates of using intact, undigested proteins. To the contrary, they teach away from it. For example, Yates expressly states: "It is believed that the present invention can be used with any size peptide. The process **requires** that peptides be fragmented and there are methods for achieving fragmentation of very large proteins." (Emphasis added.) Column 18, lines 57-60. The disclosures on Column 4 (lines 15-25 and 49-65) of the Yates patent (as cited in the Office action) refers to the fact that peptides are derived from a protein, but do not disclose the use of intact, undigested proteins for identification purposes. This is clear from the later disclosure on Column 18 (see above) that requires the utilization of peptide fragments.

Similarly, the approach described by Wang et al. involves using digested proteins. Significantly, in the article's conclusion, they state: "To this end, an integrated approach that combines separation techniques with MALDI and electrospray ionization, enzyme chemistry, tandem MS, and peptide database is being developed." Thus, enzyme chemistry – i.e., to digest the intact proteins – is considered a prominent element of their identification method.

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As indicated above, Wang et al. do not describe using sequence databases to identify microorganisms. The approach described on Page 463, Column 2, refers to “relating” the peaks in the mass spectral database to the “gene sequences that code for their production.” This is merely a correlation that is made after the fact, and is not disclosed nor suggested for the purposes of identification.

Furthermore, both Yates and Wang et al. utilize MS methods as the core of their work. As indicated on Page 3, lines 19-20 and Page 6, lines 7-8 of the specification, characterization of individual proteins can be accomplished using any suitable means, including any methods that would be available to the skilled worker.

Taken together, the combination of Wang et al. and Yates do not provide motivation and/or an expectation of success that would not have led the skilled worker to the claimed invention.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

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The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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